This Amendment under 37 C.F.R. § 1.114 is submitted in lieu of the Brief on Appeal and in response to the Office Action mailed from the U.S. Patent and Trademark Office on December 15, 2000 (Paper No. 15) in the subject application.

Please amend the application as follows:

In the Claims

Please amend Claims 1, 5, 7, 8, 12, 16, 20, 22, 23, 27, 31 and 35. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - vi).

1. (Twice Amended) A packaging cell line comprising:

a) a mammalian cell;

b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol* but not coding sequences for HIV accessory proteins, Rev response element or constitutive transport elements;

c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein; and

d) a third retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration,

wherein said packaging cell line produces a HIV-derived retroviral vector particle.

5. (Twice Amended) A packaging cell line comprising:

a) a mammalian cell;

b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol* but not coding sequences for HIV accessory proteins, Rev response element or constitutive transport elements; and

c) a second retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration.

7. (Twice Amended) A packaging cell line comprising:

a) a mammalian cell;

b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol* but not coding sequences for HIV accessory proteins, Rev response element or constitutive transport elements; and

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c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein.

8. (Twice Amended) A method of producing a packaging cell line which produces a HIV-derived retroviral vector particle, comprising co-transfecting mammalian host cells with:

a) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins but not DNA sequences encoding HIV accessory proteins, Rev response element or constitutive transport elements;

b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

c) a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration,

thereby producing a packaging cell line which produces a HIV-derived retroviral vector particle.

12. (Three Times Amended) A method of producing a HIV-derived retroviral vector particle comprising the steps of:

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a) co-transfecting mammalian host cells with:

i) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins but not DNA sequences encoding HIV accessory proteins, Rev response element or constitutive transport elements;

ii) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

iii) a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration,

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b) maintaining the transfected cells under conditions suitable for virus particle production; and

c) recovering virus particle produced in step b).

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16. (Twice Amended) A packaging cell line comprising:

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a) a mammalian cell;

b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a lentivirus *gagpol* but not coding sequences for lentivirus accessory proteins, Rev response element or constitutive transport elements;

c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein; and

d) a third retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration,

wherein said packaging cell line produces a lentivirus-derived retroviral vector particle.

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20. (Twice Amended) A packaging cell line comprising:

a) a mammalian cell;

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b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for lentivirus *gagpol* but not coding sequences for lentivirus accessory proteins, Rev response element or constitutive transport elements; and

c) a second retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration.

D6 cancel

22. (Twice Amended) A packaging cell line comprising:

a) a mammalian cell;

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b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for lentivirus *gagpol* but not coding sequences for lentivirus accessory proteins, Rev response element or constitutive transport elements; and

c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein.

23. (Twice Amended) A method of producing a packaging cell line which produces a lentivirus-derived retroviral vector particle, comprising co-transfecting mammalian host cells with:

a) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins but not DNA sequences encoding lentivirus accessory proteins, Rev response element or constitutive transport elements;

b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

c) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration,

thereby producing a packaging cell line which produces a lentivirus-derived retroviral vector particle.

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27. (Three Times Amended) A method of producing a lentivirus-derived retroviral vector particle comprising the steps of:

a) co-transfecting mammalian host cells with:

i) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins but not DNA sequences encoding lentivirus accessory proteins, Rev response element or constitutive transport elements;

ii) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

iii) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration,

b) maintaining the transfected cells under conditions suitable for virus particle production; and

c) recovering virus particle produced in step b).

31. (Three Times Amended) A HIV-derived retroviral vector particle having no viral accessory proteins produced by the method comprising the steps of:

a) co-transfecting mammalian host cells with:

i) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins but not DNA sequences encoding HIV accessory proteins, Rev response element or constitutive transport elements;

ii) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

iii) a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration; and

b) maintaining the transfected cells under conditions suitable for virus particle production.

35. (Three Times Amended) A lentivirus-derived retroviral vector particle having no viral accessory proteins, produced by the method comprising the steps of:

a) co-transfecting mammalian host cells with:

i) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins but not DNA sequences encoding lentivirus accessory proteins, Rev response element or constitutive transport elements;

ii) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

iii) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration; and

b) maintaining the transfected cells under conditions suitable for virus particle production.

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REMARKS

Rejection of Claims 1-3, 5, 7-10, 12-14, 16-18, 20, 22-25, 27-29, 31-33 and 35-37 Under 35 U.S.C. § 112, First Paragraph

Claims 1-3, 5, 7-10, 12-14, 16-18, 20, 22-25, 27-29, 31-33 and 35-37 have been rejected under 35 U.S.C. § 112, first paragraph, because, in the Examiner's assessment, the specification "does not reasonably provide enablement for embodiments wherein the first lentiviral nucleotide sequence does not comprise the gagpol sequences operatively linked to a RRE." Applicants respectfully disagree with this assessment.

The standard for enablement under 35 U.S.C. § 112, first paragraph, is whether the claimed invention can be practiced without undue experimentation given the guidance presented in the specification and what was known to the skilled artisan at the time the subject application